E-cadherin plays an essential role in collective directional migration of large epithelial sheets.

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Public Summary:
For most types of cells in our body, they tend to migration as groups. In another words, they migrate collectively. The authors have reported that for both human iPS cells and human embryonic stem cells, large groups of cells migrate together. In this paper, they investigated the difference in electric field-guided migration of single cells versus group of cells. They showed for the first time that the cells migrate significantly better in groups than in isolation. This unique property in response to electric fields offers advantage over most chemical stimulation that tend to dissociate cells.

Scientific Abstract:
In wound healing and development, large epithelial sheets migrate collectively, in defined directions, and maintain tight cell-cell adhesion. This type of movement ensures an essential function of epithelia, a barrier, which is lost when cells lose connection and move in isolation. Unless wounded, epithelial sheets in cultures normally do not have overall directional migration. Cell migration is mostly studied when cells are in isolation and in the absence of mature cell-cell adhesion; the mechanisms of the migration of epithelial sheets are less well understood. We used small electric fields (EFs) as a directional cue to instigate and guide migration of epithelial sheets. Significantly, cells in monolayer migrated far more efficiently and directionally than cells in isolation or smaller cell clusters. We demonstrated for the first time the group size-dependent directional migratory response in several types of epithelial cells. Gap junctions made a minimal contribution to the directional collective migration. Breaking down calcium-dependent cell-cell adhesion significantly reduced directional sheet migration. Furthermore, E-cadherin blocking antibodies abolished migration of cell sheets. Traction force analysis revealed an important role of forces that cells in the leading rows exert on the substratum. With EF, the traction forces of the leading edge cells coordinated in directional re-orientation. Our study thus identifies a novel mechanism--E-cadherin dependence and coordinated traction forces of leading cells in collective directional migration of large epithelial sheets.